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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/877,933	06/07/2001	Jeff Gray	014907001910	1440

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EXAMINER
HINES, JANA A

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 06/18/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/877,933	GRAY ET AL.	
	Examiner	Art Unit	
	Ja-Na Hines	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of Group I in the reply filed April 22, 2004 is acknowledged. Claims 17-31 have been cancelled. Claims 1-16 are under consideration in this office action.

Specification

2. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

3. The attempt to incorporate subject matter into this application by reference to 08/835,159 at pages 19-20 and the like as recited throughout the instant specification, is improper because a mere reference to another application, is not incorporation since the documents do not appear to be published. However, if the applications have been published, the patent number needs to be entered in place of the serial number.

4. The specification at page 20 lines 16-18 and page 21 lines 26-28 contains a blank in the sentences concerning the deposit information. When the original deposit is made after the effective filing date of an application for patent, an applicant is required to promptly submit a statement from a person in a position to corroborate that the biological material which is deposited is a biological material specifically identified in the

application (the filing date of which is relied upon) as filed. The nature of this corroboration will depend on the circumstances in the particular application under consideration, including the length of time between the application filing date and the date of deposit. While few, if any, situations can be imagined where the description requirement of 35 U.S.C. 112 can be satisfied where the biological material was not in existence at the time of filing, the rules will not preclude such a situation as there is no requirement in the patent law that an actual reduction to practice occur as a condition precedent to filing a patent application.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 7 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a deposit rejection.

The specification lacks complete deposit information for the deposit of hybridoma producing monoclonal antibodies SCPc.4.PC. Because it is not clear that cell lines

possessing the properties of SCPc.4.PC are known and publicly available or can be reproducibly isolated from nature without undue experimentation and because the claims require the use of SCPc.4.PC, a suitable deposit for patent purposes is required. Without a publicly available deposit of the above cell line, one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed. Exact replication of the cell line is an unpredictable event.

If a deposit has been made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository is required. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State. Amendment of the specification to recite the date of deposit and the complete name and full street address of the depository is required.

If the deposit has not been made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR §1.801-1.809, assurances regarding availability and permanency of deposits are required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the

authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request;

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application;

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent of or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

In addition, a deposit of biological material that is capable of self-replication either directly or indirectly must be viable at the time of deposit and during the term of deposit. Viability may be tested by the depository. The test must conclude only that the deposited material is capable of reproduction. A viability statement for each deposit of a biological material not made under the Budapest Treaty must be filed in the application and must contain:

1) The name and address of the depository;
2) The name and address of the depositor;
3) The date of deposit;
4) The identity of the deposit and the accession number given by the depository;
5) The date of the viability test;
6) The procedures used to obtain a sample if the test is not done by the depository; and
7) A statement that the deposit is capable of reproduction.

As a possible means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If the deposit was made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to

corroborate that the hybridoma cell line described in the specification as filed is the same as that deposited in the depository. Corroboration may take the form of a showing of a chain of custody from applicant to the depository coupled with corroboration that the deposit is identical to the biological material described in the specification and in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundack*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR §1.801-1.809 for further information concerning deposit practice.

6. Claims 2,3 and 16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method of detection comprising detecting the protein disulfide isomerase comprising amino acid sequence an amino acid sequence at least ten consecutive amino acids of which are substantially identical to a subsequence of an amino acid sequence SEQ ID NO:3 or the protein disulfide isomerase that has an amino acid sequence that is substantially identical to the amino acid sequence of SED ID NO:2.

The specification does not provide functional or structural characterization of the protein disulfide isomerase's comprising amino acid sequence an amino acid sequence at least ten consecutive amino acids of which are substantially identical to a subsequence of an amino acid sequence SEQ ID NO:3 or a protein disulfide isomerase

(PDI) that has an amino acid sequence that is substantially identical to the amino acid sequence of SED ID NO:2 as instantly claimed. The specification does not provide a clear protocol by which the PDI that has least ten consecutive amino acids of which are substantially identical to a subsequence of an amino acid sequence SEQ ID NO:3 or a protein disulfide isomerase (PDI) that has an amino acid sequence that is substantially identical to the amino acid sequence of SED ID NO:2 has been isolated at the time the invention was made. The specification does not provide structural characterization of the of said peptides. The specification alleges functionality as capable of biding to a capture reagent, with no evidence supported by the instant specification. In view of the lack of evidence in the specification as filed, it is apparent that one skilled in the art would recognize that applicants were not in possession, at the time of filing the instant application, of PDI's having at least ten consecutive amino acids of which are substantially identical to a subsequence of an amino acid sequence SEQ ID NO:3 or PDI's that have an amino acid sequence that is substantially identical to the amino acid sequence of SED ID NO:2. Absent characterization of the claimed PDI's, the genus of peptides or immunological variants is highly diverse and applicants have failed to describe such variants.

In view of these considerations, a person of skill in the art would not have viewed the teachings of the specification sufficient to show that Applicants were in possession of PDI having at least ten consecutive amino acids of which are substantially identical to a subsequence of an amino acid sequence SEQ ID NO:3 or PDI's that have an amino

acid sequence that is substantially identical to the amino acid sequence of SED ID NO:2 as asserted in the specification and claims.

7. Claims 2-3 and 16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "substantially identical" in claims is a relative term which renders the claim indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. IT is unclear how much identity is required for a sequence to be substantially identical. Therefore the metes and bounds of the claims are not clear and clarification is required to overcome the rejection.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

8. Claims 1,3-6 and 8-15 are rejected under 35 U.S.C. 103(a) as being unpatentable over Anusz et al., in view of Blunt et al.

The claims are directed to a method of diagnosing infection of a mammal by a *Cryptosporidium* species, the method comprising: contacting a stool sample with a capture reagent which binds to PDI and detecting whether the PDI is bound to the capture reagent wherein its presence is indicative of *Cryptosporidium* infection. The dependant claims are drawn to the capture reagent and detection agent. Claims 14-15 are drawn to kit for diagnosing infection of a mammal by a *Cryptosporidum* species comprising a solid support, a detection reagent, and positive control.

Anusz et al., teach the detection of *C.parvum* in bovine feces by monoclonal antibody capture enzyme-linked immunosorbent assay (ELISA). Diagnosis can be based on the detection of fecal oocysts using methods such as: concentration, staining of fecal smears, latex agglutination, and immunofluorescence using monoclonal and polyclonal antibodies (page 2770). The materials and methods section teaches the production of polyclonal and monoclonal antibodies (page 2770). It is noted that antibodies can be prepared by any techniques including techniques using DNA methodologies. Anusz et al., teach the use of a solid support upon which immobilizes a capture reagent, such as an antibody that binds and detects antigen (page 2771). ELISA plates were purchased from a vendor (page 2771). Anusz et al., teach the production of polyclonal and monoclonal antibodies to *C.parvum* (page 2771). The flat bottom plates were coated with monoclonal antibody (page 2771). The performance of the ELISA teaches the use of the peroxidase conjugated rabbit anti-goat detection antibody and they were scored using an automated plate reader (page 2771). Thus Anusz et al., teach a double antibody sandwich ELISA. The fecal samples were added

to the appropriate wells and tested (page 2771). Detectable labels taught by Anusz et al, include peroxidase and immunofluorescence labels. It is noted that the ELISA plates and detection reagents where brought as commercial kits and come with instructions for use (page 2771). However, Anusz et al., do not teach the use of a reagent which specifically binds to a protein disulfide isomerase of *C.parvum*.

Blunt et al., teach the sequence of the parasitic protozoan *C.parvum*, putative protein disulfide isomerase-encoding DNA. The protein disulfide isomerase has a high degree of homology to protein disulfide isomerase's from other species (abstract). The library was screened with rat antiserum against a homogenate of purified *C.parvum* oocysts and sporozoties (page 221). Blunt et al., also teach using comparisons of the deduced amino acid sequence using the BLASTP program (page 221). Figure 1 teaches the deduced amino acid sequence. Moreover, the amino acid sequence of Blunt et al., shows greater then 90% sequence identity to SEQ ID NO:2.

Therefore, no more than routine skill would have been required at the time of applicants invention to use the protein disulfide isomerase as taught by Blunt et al., in the detection kit of Anusz et al., because to thereby detect is presence which is indicative of infection. No more than routine skill is required to generate antibodies for a protein known in the art to be indicative of *C.parvum*. Thus, one of ordinary skill in the art would have been motivated to use alternative and/or functionally equivalent antibodies which are capable of detecting *C.parvum* in a diagnostic method with a reasonable expectation of success. Moreover, one of ordinary skill would have been motivated to use the protein disulfide isomerase in the assay to avoid the use of

infectious oocysts agents in a diagnostic assay when the use of such purified proteins will yield a higher sensitivity and specificity in diagnostic methods.

With respect to the detection kit, no more then routine skill would have been required at the time of applicants invention to modify the detection kit of Anusz et al., to incorporate the PDI as taught by Blunt et al., because Blunt et al., teach that PDI can detect *C.parvum.* Only routine skill would have been required to generate antibodies for use in an immunoassay to detect *C.parvum* infection since one of ordinary skill would have been motivated to use the protein disulfide isomerase in the assay to avoid the use of infectious oocysts agents. Furthermore, kits provide convenience to the consumer wherein the assembly of an immunoassay reagent kit is routine in the art.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached on Monday-Thursday and alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Ja-Na Hines JH
June 15, 2004

L. F. Smith
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